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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	16

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/839,894	Applicant(s) ALTBOUM ET AL.	
	Examin r Zachariah Lucas	Art Unit 1648	

-- Th MAILING DATE of this communication app ars on th cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *2-9,17-34,36-47 and 51-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12-16,35 and 48-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *26 November 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1-81 are pending in the present application. Claims 2-9, 17-34, 36-47, and 51-81 are withdrawn from consideration as to non-elected inventions. Claims 1, 10-15, 35, and 48-50 are under consideration.

2. It is noted that claim 16 was erroneously included in the claims examined in the prior action. Prior to amendment filed on November 26, 2002, this claim read on a non-elected invention, i.e. compositions referring not to polypeptides, but to polynucleotides. As there are different issues involved between these types of molecules, and as the claims cover disparate subject matter, the subject matter of claim 16 as claimed does not belong in the same restriction Group as the remaining elected claims. Although the subject matter of the claim presently includes the elected subject matter, should the claim be amended back to its original form, it would be withdrawn from examination as to a non-elected invention.

3. In view of the new rejection raised in this action, the action is being made Non-Final.

Specification

4. **(Prior Objections-Withdrawn)** The disclosure was objected to in the office action mailed July 30, 2002 (the prior action) for various informalities. In view of the amendments made to the specification in the response filed November 26, 2002 (Amend. A), the objections are hereby withdrawn.

Drawings

5. In the prior action, the Figures 2A and 2Bwere objected to for not identifying the parA section of the disclosed plasmids. The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on November 26, 2002 have been approved by the examiner with respect to the subject matter enclosed therein. A proper drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. **(New Rejection- Necessitated by Amendment)** Claim 16 as amended is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim has been amended to read on an immunogenic composition comprising a carrier comprising a *csa* operon. However, the application does not disclose such a carrier. The claim is therefor rejected for reading on new matter to the application.

8. **(New Rejection)** Claims 1, and 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. These claims read on immunogenic compositions comprising products of the *csa* operon. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "recombinant product" in claim 1 is defined by the application to include "the *csa* operon itself" (page 6, lines 3-4). In view of the subject matter of claim 16 as files, the term also apparently reads on other forms of nucleic acids. However, the accepted meaning of a product of an operon, or any other nucleic acid, is the protein or peptide that is produced upon expression of the polynucleotide See e.g. Watson et al., Recombinant DNA, page 49, and CancerWEB Online Medical Dictionary, "gene product." In short, while the product of a nucleic acid may include RNA molecules, it is normally considered to be the encoded protein. The product of a nucleic acid is not considered to include itself or a fragment of itself. Thus, the claims are rejected for indefiniteness.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. **(Prior rejection –Maintained)** Claims 1, 10-11, 35, and 48-50 were rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by McConnell et al., Infection and Immunity, 56:1974-1980 (McConnell), and Rudin et al, Microbial Pathogenesis, 16:131-139 (Rudin) These claims describe an immunogenic composition comprising csaA

As stated in the prior action, McConnell teaches that CS4 expressing E. coli were able to produce antibodies to CS4. p. 1975. Because the article discloses the entire CS4 as an immunogen, it also inherently discloses an immunogenic composition comprising the CsaE subunit. The applicant traverses this rejection on that the reference does not teach the isolation of the CS4 operon or *csaE*. The applicants' traversal is not found persuasive because the claims read on the recombinant *product* of the operon, not the operon itself. As the application does not identify any distinguishing characteristics between the CS4 fimbria in nature and the recombinant product, the source of the antigen is not deemed pertinent to patentability. This is further supported by the sentence of lines 12-15 on page 18 of the specification. This sentence states that proteins from both naturally occurring and from recombinant sources are encompassed by the description of the application. Thus, the source of the protein is not deemed relevant.

The applicant also traverses the rejection because the reference does not teach the purified polypeptide sequence of the recombinant operon. As stated in the prior action, the reference does disclose the E11881A ETEC as a strain producing the CS4 antigen, and indicates that this strain was tested in the experiments run in the reference. See Table 1; and page 1975 (describing that the ELISA assay of the bacterium was conducted with denatured cells in saline, which could be considered an immunogenic composition). As the protein described by the reference is from the same strains as bacteria as the claimed product, it is reasonable to assume that the protein sequence is identical, or at least within the 95% homology permitted by the claims.

The relevance of the remainder of the applicant's argument against McConnell, relating to the lack of a definitive teaching relating to the operons for the CS4 and CS6 fimbria, is not

understood. The present claims are not directed to a plasmid vector comprising the coding regions for both the CS4 and CS6 fimbria. Rather, the claims relate only to an immunogenic composition comprising the csaE portion of the CS4 fimbria or to any product of the *csa* operon. The *csa* operon is taught by the present specification to encode the proteins of the CS4 fimbria. Page 7, lines 18-21, and page 9, line 13 to page 10, line2. Thus, a composition comprising the CS4 antigen is a product of the operon regardless of whether the operons of the CS4 and CS6 fimbria are present on the same plasmid. It is therefore unclear what the relevance of the physical relationship of the CS4 and CS6 coding regions is to the rejected claims.

The applicant's traversal of Rudin is also on the basis that the reference does not teach the isolated genes or the protein sequence. These facts are not deemed dispositive for the reasons stated above in the discussion regarding McConnell.

11. **(Prior Rejection –Maintained)** Claims 1, 12-15, and 35 were rejected in the prior action under 35 U.S.C. 102(b) as being anticipated by WO 96/38171, naming Cassels et al. as inventors (Cassels). Claim 1 describes an immunogenic composition comprising a recombinant product of a *csa* operon and a carrier. Claim 35 describes a purified polypeptide sequence expressed from a recombinant *csa* operon. It is noted that the applicant has amended the claim to remove the language "or an antigenic fragment thereof." It is assumed that the intent of this amendment was to avoid the rejection by limiting the claim to full length sequences. However, the term polypeptide is not being read as meaning the full length csa proteins. See App., pp. 18-19. Polypeptides are disclosed in the application as having sequences substantially the same as the sequences of SEQ ID NOs: 2, 4, 6, 8, and 10, or fragments of these sequences. Id. The

application continues by defining "substantially the same" as meaning polypeptides of various percent homologies to a reference amino acid, and states that "for polypeptides, the length of comparison sequences will generally be at least 16 amino acids..." Thus, according to the specification, the term polypeptide is not limited to full length amino acid sequences of the disclosed proteins.

The applicant traverses this rejection for two reasons. First, the applicant argues that the rejected claims are directed to the *csa* operon, and/or to the *csa*E gene. This is incorrect. The claims are directed to a recombinant product of these nucleic acids. As was stated in the prior action, and again above, the source of the polypeptide products of these claims is not deemed relevant to the patentability of the polypeptide as the applicant has not established that the source of the polypeptide has any effect on the operation of the product.

The applicant also argues that "a peptide synthesizer cannot even generate o protein as larger as *csaE*." It is assumed that the applicant intended to refer to the csaE protein, rather than to the *csaE* gene. It is also noted that the rejection over Cassels does not extend to claims 10 or 11, which read on the full length sequence. They are limited to the generic claims to an immunogenic composition comprising "a recombinant product." The term recombinant product is not limited to the full length of the csaE protein. See e.g., App. page 33, lines 16-20, stating that small fragments of the product of the *csa* operon may be used to provide an immunogenic composition. The disclosure further states that such fragments may be between 5 to 30 amino acids in length. Thus, the claims may read to include immunogenic compositions comprising only fragments of the disclosed proteins. In view of this, the applicant's arguments regarding the

inability of a peptide synthesizer to produce a full length sequence is not deemed relevant to the rejection made.

12. **(Prior Rejection- Withdrawn)** Claim 16 was rejected in the prior action under 35 U.S.C. 102(b) as anticipated by McConnell or, in the alternative, under 35 U.S.C. 103(a) as obvious over McConnell, in view of U.S. Patent Number 5,932,715, issued to Scott et al (Scott); or optionally in view of Lodish et al., excerpt from a Molecular Cell Biology text (Lodish), and further in view of Scott. Claim 16 has been amended to read on an immunogenic composition comprising a recombinant product of a *csa* operon and a carrier comprising the *csa* operon. As the reference does not disclose such a composition, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. **(Prior Rejection –Maintained)** Claims 12-15 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over McConnell in view of Cassels. For the purposes of this rejection, the claims are being read as to the immungenic compositions of claims 12-15 wherein the peptides are those taught by McConnell.

The applicant traverses the rejection on the grounds that cited reference do not teach recombinant products of the *csa* operon. The examiner disagrees for the reasons stated above with respect to the anticipation rejection over McConnell. As the applicant has provided no further reason for traversing the rejection, it is maintained.

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
January 30, 2003

JAMES HOUSEL 2/10/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600